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CHANGES IN LEUKOCYTES AND ALKALI RESERVE OF BLOOD IN EXPERIMENTAL INFECTIONS

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Methods for estimating quantitatively the alkali reserve of the blood depend on determining the carbon dioxid binding power of either whole blood or blood plasma after saturation with air or gas mixtures containing a definite concentration of carbon dioxid. The results, while expressing only a part of the entire alkali reserve, are accepted generally as an index of the chemical condition of the blood, a diminution below the normal carbon dioxid binding power being regarded as acidosis. Diminished alkali reserve of the blood has been observed in the acidosis of diabetes and uremia, also in pneumonia and in other acute infectious diseases. There seems to be no observations at hand in regard to the alkali reserve changes in the blood in experimental infections with parallel observations of the variation in the number of leukocytes. The results of such a study in rabbits are contained in this report.

Living cultures of various bacteria were injected intravenously into rabbits, and at short intervals thereafter the animals were bled from the ear vein, and the alkali reserve of the whole blood was determined with a portion of the blood, the number of leukocytes with another portion taken directly from the bleeding vessel. Injections with the following bacteria were made: B. typhosus, B. dysenteriae-(Flexner), B. coli, Streptococcus hemolyticus, Streptococcus viridans, B. diphtheriae, B. pneumoniae, and B. welchii. These bacteria were grown in pure culture on suitable plain or blood-agar slants, the growth after 18 to 24 hours' incubation suspended in sterile normal salt solution, and the suspension injected intravenously, the fluid volume injected not exceeding 2.5 c.c. The alkali reserve of the whole blood was determined according to the Van Slyke and Cullen[1] method after equilibration with air containing 5.5% carbon dioxid, and the readings obtained were corrected for 0 C. and 760 mm. barometric pressure.

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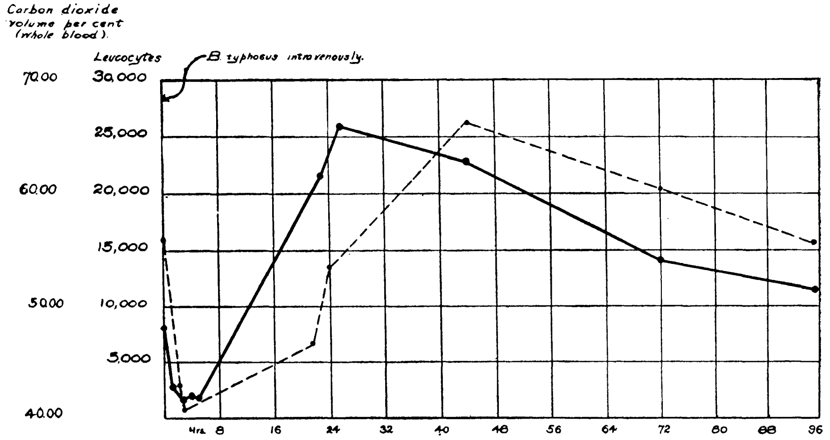
[1] J. Biol. Chem., 1917, 30, p. 289.

Within 2 to 4 hours after the injection of the suspension of the bacteria, the leukocytes of the blood rapidly diminish in number, in some rabbits decreasing to 1,000 to 2,000 per cmm. Coincidently, the carbon dioxid binding power of the blood diminishes rapidly, its lowest level being reached shortly after the minimum attained by the leukocytes. During the succeeding 12 to 18 hours there is a rapid increase in the number of leukocytes, and a return to normal of the blood alkali reserve, the latter lagging somewhat behind the former. A marked leukocytosis is preceded by a marked and comparatively long continued depression of the blood alkali reserve. This low alkali reserve is followed by a rebound to a higher than normal value (alkalinosis) of short duration, and then a gradual return to normal with the return to normal of the number of leukocytes.



Illustrating the changes in the number of leukocytes and in the alkali reserve of the blood following an intravenous injection of living typhoid bacilli. The continuous black line indicates leukocytes; the broken line the alkali reserve.

The recovery of the alkali reserve and the rise in the number of leukocytes of the blood is not always parallel. The curves usually are parallel when the return to normal of each takes place within 48 to 72 hours. In experiments in which the maximum leukocytosis is not accompanied or followed shortly by a prompt return to normal of the blood alkali reserve, the latter remains depressed and the leukocytes continue high. Later, with the alkali reserve returning to normal, the number of leukocytes decreases and the curves tend to become parallel. Rabbits with only a slight depression of their blood alkali reserve have little or no variation in the number of their leukocytes.

Results of Experiments with Various Bacteria

Time	Colon Bacillus		Dysentery Bacillus		Typhoid Bacillus		Hemolytic Streptococcus		Streptococcus Viridans		Pneumococcus		Staphylococcus		Diphtheria Bacillus		Friedländer Bacillus		Bacillus Welchii	
	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes	Alkali Reserve	Leukocytes
Before injection	64.88	11,200	65.58	7,500	67.46	12,100	68.76	9,800	55.78	9,500	55.72	7,700	63.97	7,200	66.04	11,300	58.94	8,400	66.81	15,000
1 hour	......	......	......	......	......	......	64.24	6,000	53.97	3,400	......	......	......	5,500	64.37	6,300	48.96	2,500		
2 hours	42.83	2,000	50.65	1,900	39.30	3,600	55.29	6,400	50.26	......	......	......	61.21	......	64.20	......	51.64	1,600	66.81	10,800
3 hours	41.18	2,700	......	......	19,41	9,300	......	......	46.64	......	41.29	1,400	53.97							
4 hours	45.74	3,700	......	......	25.75	7,700	......	......	50.26	3,900	......	......	56.64	10,100	52.95	6,900	44.35	800	61.60	14,700
5 hours	50.38	12,600	43.13	3,100	32.09	7,000	48.99	5,000	......	......	......	......	......	......	......	......	45.21	1,600		
6 hours	46.70	8,400	37.57	3,500	25.75	14,500	......	......	......	......	......	......	......	......	49.29	4,100	45.69	2,100		
7 hours	50.48	8,000	42.26	2,300	dead		......	......	......	......	......	......	......	......	......	......	53.99	12,100	62.17	7,200
8 hours	......	......	40.01	9,300	......	......	......	......	......	......	......	......	......	......	......	......	48.49	22,500		
9 hours	......	......	......	......	......	......	......	......	......	......	......	......	......	......	55.29	4,300	48.49	7,000		
10 hours	......	......	......	......	......	......	......	......	......	......	......	......	......	......	......	......	43.95	10,400		
19 hours	48.55	27,700	......	......	......	......	......	......	......	......	......	......	......	......	......	......	......	26,000		
20 hours	......	......	......	......	......	......	......	......	55.21	12,900										
21 hours	50.39	25,200	......	......	......	......	80.50	20,000												
22 hours	48.55	23,600	51.33	20,300	......	......	......	......	......	......	55.11	28,700	57.17	8,300	......	......	......	......	65.85	13,000
23 hours	......	......	......	......	......	......	......	......	......	......	......	......	......	......	73,60	10,800	57.47	24,800		
24 hours	......	......	......	......	......	......	67.59	20,000	54.43	10,500										
26 hours	......	......	55.34	19,000	......	......	63.02	12,400	......	......	......	......	......	......	......	......	63.17	17,000		
2 days	67.44	24,500	......	......	......	......	61.79	10,500	58.63	10,300	......	......	59.31	9,000	55.69	10,100				
3 days	65.47	21,100	67.30	12,800	......	......	......	......	......	......	......	......	......	......	69.62	17,100	52.02	23,400		
4 days	45.79	28,000	63.60	14,600	......	......	54.82	10,200	......	......	......	......	......	......	69.29	16,700	65.07	10,800		
5 days	47.04	22,000	56.89	10,200	......	......	......	......	......	......	......	......	......	......	61.78	11,300				
6 days	55.00	18,000	......	......	......	......	59.83	11,600												
7 days	56.90	14,000																		
8 days	65.34	24,300																		
9 days	57.72	15,000																		
12 days	57.72	9,000																		

The chart represents graphically the alkali reserve changes and the variation in the number of leukocytes of the blood following an injection of typhoid bacteria. The curves illustrating these changes in rabbits injected with other bacteria are comparable. The table contains the data obtained in the individual experiments with various bacteria other than the one given in the chart.

Control rabbits receiving sterile salt solution or broth up to 6 c c intravenously manifest no change in their blood alkali reserve or in the number of leukocytes. Other factors such as handling of the animals, environment, and the amount of blood drawn have been controlled and found to have no results such as those given for the injections of bacteria.

DISCUSSION

The mobilization of leukocytes at the site of infected tissues because of chemical substances produced or liberated by bacteria is well known. Many substances have been found to exert locally a positive chemotactic influence on leukocytes, others a negative.[2] The results obtained in my experiments indicate that a general leukocytosis and leukopenia are accompanied by definite chemical changes of the blood. It is possible that the factors lowering the alkali reserve, or that the lowered alkali reserve itself (acidosis) furnish the chemical stimulus necessary for the production of leukocytosis. The results obtained seem to indicate that the degree of leukocytosis is in ratio not so much with the extent of the initial leukopenia as it is with the degree of alkali reserve depression and the length of time during which it is depressed.

CONCLUSIONS

The intravenous injection of living bacteria into rabbits usually causes, within a period of 2 to 4 hours, a leukopenia and a diminution of the blood alkali reserve. There follows a rise in the number of leukocytes and a return to normal of the alkali reserve. There may be a short period of alkalinosis. The minimal and maximal alkali reserve levels are reached after a corresponding leukopenia and leukocytosis. Continued low alkali reserve is accompanied by a persistently high leukocytosis. With the rise to normal of the alkali reserve there is a decline in the number of leukocytes. It is suggested that diminution of the alkali reserve, or the factors associated with this depression, may afford the chemical stimulus necessary for the subsequent leukocytosis.

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[2] Wells, H. G.: Chemical Pathology, 1920, p. 250.